Title

Transient improvement of urticaria induces poor adherence as assessed by Morisky Medication Adherence Scale-8.

Journal

The Journal of dermatology, 42(11)

ISSN

0385-2407

Authors

Kaneko, Sakae
Masuda, Koji
Hiragun, Takaaki
et al.

Publication Date

2015-11-01

DOI

10.1111/1346-8138.12971

Peer reviewed

JDA Japanese Dermatological Association
The Journal of Dermatology

doi: 10.1111/1346-8138.12971 *Journal of Dermatology* 2015; **42**: 1078–1082

CONCISE COMMUNICATION

Transient improvement of urticaria induces poor adherence as assessed by Morisky Medication Adherence Scale-8

Sakae KANEKO,[1] Koji MASUDA,[2] Takaaki HIRAGUN,[3] Naoko INOMATA,[4] Masutaka FURUE,[5] Daisuke ONOZUKA,[6] Satoshi TAKEUCHI,[7] Hiroyuki MUROTA,[8] Makoto SUGAYA,[9] Hidehisa SAEKI,[10] Yoichi SHINTANI,[11] Yuichiro TSUNEMI,[12] Shinya ABE,[13] Miwa KOBAYASHI,[14] Yuki KITAMI,[15] Miki TANIOKA,[16] Shinichi IMAFUKU,[17] Masatoshi ABE,[18] Akihito HAGIHARA,[6] Donald E. MORISKY,[19] Norito KATOH[2]

[1]Department of Dermatology, Shimane University Faculty of Medicine, Shimane, [2]Department of Dermatology, Kyoto Prefectural University of Medicine Graduate School of Medical Science, Kyoto, [3]Department of Dermatology, Integrated Health Sciences, Institute of Biomedical and Health Sciences, Hiroshima University, Hiroshima, [4]Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Kanagawa, [5]Department of Dermatology, [6]Department of Health Care Administration and Management, Kyushu University Graduate School of Medical Sciences, [7]Department of Dermatology, Federation of National Public Service Personnel Mutual Aid Associations, Hamanomachi Hospital, Fukuoka, [8]Department of Dermatology, Graduate School of Medicine, Osaka University, Osaka, [9]Department of Dermatology, Faculty of Medicine, University of Tokyo, [10]Department of Dermatology, Nippon Medical School, Tokyo, [11]Department of Geriatric and Environmental Dermatology, Nagoya City University Graduate School of Medical Sciences, Nagoya, [12]Department of Dermatology, Tokyo Women's Medical University, Tokyo, [13]Department of Dermatology, Kanazawa Medical University, Ishikawa, [14]Department of Dermatology, University of Occupational and Environmental Health, Fukuoka, [15]Department of Dermatology, Showa University School of Medicine, Tokyo, [16]Tanioka Dermatology Clinic, Kyoto, [17]Department of Dermatology, Faculty of Medicine, Fukuoka University, Fukuoka, [18]Sapporo Skin Clinic, Hokkaido, Japan, [19]Department of Community Health Sciences, UCLA Fielding School of Public Health, Los Angeles, CA, USA

ABSTRACT

Poor adherence to medication is a major public health challenge. Here, we aimed to determine the adherence to oral and topical medications and to analyze underlying associated factors using the translated Japanese version of Morisky Medication Adherence Scale-8 regarding urticaria treatment. Web-based questionnaires were performed for 3096 registered dermatological patients, along with a subanalysis of 751 registered urticaria patients in this study. The adherence to oral medication was significantly associated with the frequency of hospital visits. Variables that affected the adherence to topical medication included age and experience of drug effectiveness. The rate of responses that "It felt like the symptoms had improved" varied significantly among the dermatological diseases treated with oral medications. Dermatologists should be aware that adherence to the treatment of urticaria is quite low. Regular visits and active education for patients with urticaria are mandatory in order to achieve a good therapeutic outcome by increasing the adherence.

Key words: **adherence, oral, topical, transient improvement, urticaria.**

INTRODUCTION

Urticaria is one of the most common skin diseases and is characterized by the appearance of itchy wheals and flares that usually disappear within hours.[1] "Spontaneous urticaria" is the most common type, in which wheals develop spontaneously over the course of a day. It consists of acute (spontaneous) urticaria and chronic (spontaneous) urticaria, in which wheals occur for less than 6 weeks or 6 weeks or more, respectively.[2] In Japan, the term "chronic urticaria" is used to represent, on some occasions, urticaria that continues for more than 1 month regardless of the presence of triggers.[1]

The medication adherence of patients with acute urticaria does not seem to affect the outcome, because it is usually self-limiting. However, in chronic urticaria, poor adherence often results in the failure of treatment and the relapse of symptoms. Recently, an eight-item self-reporting scale was developed by Morisky *et al.*,[3] called the Morisky Medication Adherence Scale-8 (MMAS-8). Although this scale originally targeted oral medication for hypertensive patients, we recently assessed the medication adherence for oral and topical remedies using a translated Japanese version of MMAS-8.[4,5] We also performed a subanalysis of 751 registered patients with urticaria in this study.

Correspondence: Sakae Kaneko, M.D., Department of Dermatology, Shimane University Faculty of Medicine, 89-1 Enya-cho, Izumo City, Shimane 693-8501, Japan. Email: kanekos2@med.shimane-u.ac.jp
Received 16 March 2015; accepted 26 April 2015.

METHODS

This study was conducted among patients registered in a monitoring system established by Macromill (Tokyo, Japan) which has been described elsewhere.[4,5] Our Web-based questionnaire included questions on the following items: age, sex, marital status, annual income, employment status, educational status, smoking habit, alcohol consumption, frequency of hospital visits, disease duration, main health-care institution, oral or topical medication, experience of the effectiveness of oral medication, experience of the effectiveness of topical medication, experience of adverse events associated with oral medication, experience of adverse events associated with topical medication and overall satisfaction with treatment, as well as MMAS-8 for oral medication and MMAS-8 for topical medication.

The characteristics of the whole sample and of the groups with different levels of adherence in terms of the MMAS-8 score are presented. The χ^2-test for categorical variables or ANOVA for continuous variables was used to evaluate the differences in the study variables among the three adherence groups. Internal consistency was assessed using Cronbach's alpha. An acceptable Cronbach's alpha value is considered to be 0.7 or more.[6] Known group validity was assessed through the association of items and MMAS categories using correlation coefficient and covariance. All analyses were performed using STATA version 9 (StataCorp, College Station, TX, USA). The significance level was set at $P < 0.05$.

RESULTS

Demographic data of the 751 patients with urticaria are summarized in Table 1. The mean age of these subjects was 45.4 years (range, 17–80) and 33.6% of them were male. Among these 751 patients, a total of 673 took oral medication and 528 were treated with topical medication. Mean adherence scores by MMAS-8 were 4.9 for oral and 4.2 for topical medication. The reliability scores (i.e. Cronbach's alpha) were 0.683 for oral MMAS-8 and 0.726 for topical MMAS-8, which demonstrated moderate to high reliability of the Japanese version of MMAS-8.

As shown in Table 2, the adherence to oral medication was significantly associated with the frequency of hospital visits. Variables that affected the adherence to topical medication were age, disease duration and experience of drug effectiveness.

Among the 673 urticaria patients with oral drugs, 75 (11.1%) admitted that they ignored doctors' instructions, whereas 124 of the 528 (23.5%) urticaria patients with topical remedies did so. Although 29.0% (36/124) of patients stopped applying topical remedies because they thought their lesion had been cured, significantly more patients (48.0%; 36/75) stopped oral drugs due to the same reason, suggesting that the adherence to oral drugs could be affected more by patients' own decisions regarding continued medication use (Table 3). Factors that influence adherence to oral and topical medication were investigated. Patients' reasons for not adhering to their

Table 1. Basic characteristics of urticaria patients (n = 751)

Characteristics	*n*	%
Age, mean (SD, range), years	45.4 (11.7, 17–80)	
Sex		
Male	252	33.6
Female	499	66.4
Marital status		
Married	270	36.0
Unmarried	481	64.0
Annual income		
≥¥6 million	266	40.6
<¥6 million	389	59.4
Employment		
Employed	453	62.8
Unemployed	268	37.2
Education		
University graduate	306	41.1
Not university graduate	439	58.9
Smoking		
Smoker	147	19.7
Non-smoker	600	80.3
Alcohol		
≥Once a month	430	57.6
<Once a month	317	42.4
Frequency of MD visits		
≥Once a half-year	637	84.8
<Once a half-year or unknown	114	15.2
Disease duration		
<Half a year	179	23.8
≥Half a year to 1 year	169	22.5
>1–3 years	168	22.4
>3–5 years	71	9.5
>5–10 years	79	10.5
>10–20 years	45	6.0
>20 years	40	5.3
Main health-care institution		
University hospital	25	3.4
Municipal hospital	135	18.1
Private clinic or other	586	78.6
Oral medication		
Experience of drug effectiveness		
Yes	611	90.8
No	62	9.2
Experience of adverse events		
Yes	124	18.4
No	549	81.6
Topical medication		
Experience of drug effectiveness		
Yes	443	83.9
No	85	16.1
Experience of adverse events		
Yes	51	9.7
No	477	90.3
Overall satisfaction with treatment		
>Satisfied	440	58.6
<Satisfied	311	41.4
Adherence, mean (SD, range)		
Oral medication	4.9 (1.9, 0.25–8)	
Topical medication	4.2 (2.1, 0–8)	
Cronbach's alpha of adherence measure		
Oral medication	0.683	
Topical medication	0.726	

SD, standard deviation.

Table 2. Prevalence of study variables for the three adherence levels among urticaria patients: oral and topical medication

Characteristics	Oral medication (n = 673)				Topical medication (n = 528)			
	High adherence n = 62 (9.2%)	Medium adherence n = 171 (25.4%)	Low adherence n = 440 (65.4%)	P	High adherence n = 33 (6.3%)	Medium adherence n = 97 (18.4%)	Low adherence n = 398 (75.4%)	P
Age, mean (SD), years	47.7 (10.8)	46.0 (11.2)	45.0 (12.1)	0.194	48.6 (11.2)	47.8 (12.4)	44.9 (12.3)	0.041
Sex								
Male	23 (10.3)	57 (25.5)	144 (64.3)	0.792	8 (4.6)	35 (20.1)	131 (75.3)	0.458
Female	39 (8.7)	114 (25.4)	296 (65.9)		25 (7.1)	62 (17.5)	267 (75.4)	
Marital status								
Married	18 (7.4)	60 (24.6)	166 (68.0)	0.384	10 (5.1)	37 (18.9)	149 (76.0)	0.698
Unmarried	44 (10.3)	111 (25.9)	274 (63.9)		23 (6.9)	60 (18.1)	249 (75.0)	
Annual income								
≥¥6 million	26 (11.0)	60 (25.4)	150 (63.6)	0.591	12 (6.7)	33 (18.5)	133 (74.7)	0.836
<¥6 million	30 (8.5)	91 (25.8)	232 (65.7)		16 (5.7)	49 (17.4)	217 (77.0)	
Employment								
Employed	33 (8.0)	107 (26.1)	270 (65.9)	0.348	15 (4.8)	60 (19.3)	236 (75.9)	0.100
Unemployed	27 (11.5)	60 (25.5)	148 (63.0)		18 (9.2)	30 (15.4)	147 (75.4)	
Education								
University graduate	22 (7.9)	74 (26.6)	182 (65.5)	0.616	12 (5.6)	44 (20.4)	160 (74.1)	0.536
Not university graduate	39 (10.0)	97 (24.9)	254 (65.1)		21 (6.8)	52 (16.9)	235 (76.3)	
Smoking								
Smoker	10 (7.8)	33 (25.8)	85 (66.4)	0.822	6 (5.4)	22 (19.6)	84 (75.0)	0.861
Non-smoker	52 (9.6)	138 (25.5)	352 (64.9)		27 (6.6)	75 (18.2)	310 (75.2)	
Alcohol								
≥Once a month	33 (8.6)	87 (22.8)	262 (68.6)	0.104	18 (5.9)	49 (16.1)	238 (78.0)	0.190
<Once a month	29 (10.1)	84 (29.2)	175 (60.8)		15 (6.8)	48 (21.9)	156 (71.2)	
Frequency of hospital visits								
≥Once a half-year	60 (10.3)	136 (23.4)	386 (66.3)	0.001	29 (6.6)	76 (17.2)	336 (76.2)	0.276
<Once a half-year or unknown	2 (2.2)	35 (38.5)	54 (59.3)		4 (4.6)	21 (24.1)	62 (71.3)	
Disease duration								
<Half a year	16 (10.3)	47 (30.1)	93 (59.6)	0.311	17 (11.5)	28 (18.9)	103 (69.6)	0.017
≥Half a year to 1 year	8 (5.8)	40 (29.0)	90 (65.2)		4 (3.1)	28 (21.4)	99 (75.6)	
>1–3 years	15 (9.4)	36 (22.6)	108 (67.9)		6 (5.4)	24 (21.6)	81 (73.0)	
>3 years	23 (10.5)	48 (21.8)	149 (67.7)		6 (4.4)	17 (12.3)	115 (83.3)	
Main health-care institution								
University hospital	3 (13.0)	5 (21.7)	15 (65.2)	0.859†	0 (0.0)	5 (29.4)	12 (70.6)	0.474†
Municipal hospital	10 (8.6)	27 (23.1)	80 (68.4)		6 (6.5)	20 (21.5)	67 (72.0)	
Private clinic or other	48 (9.1)	139 (26.2)	343 (64.7)		27 (6.5)	69 (16.6)	319 (76.9)	
Experience of drug effectiveness								
Yes	58 (9.5)	157 (25.7)	396 (64.8)	0.575	30 (6.8)	88 (19.9)	325 (73.4)	0.049
No	4 (6.5)	14 (22.6)	44 (71.0)		3 (3.5)	9 (10.6)	73 (85.9)	
Experience of adverse events								
Yes	10 (8.1)	32 (25.8)	82 (66.1)	0.887	2 (3.9)	10 (19.6)	39 (76.5)	0.864†
No	52 (9.5)	139 (25.3)	358 (65.2)		31 (6.5)	87 (18.2)	359 (75.3)	
Overall satisfaction with treatment								
>Satisfied	37 (9.4)	109 (27.8)	246 (62.8)	0.205	22 (7.0)	60 (19.1)	232 (73.9)	0.558
<Satisfied	25 (8.9)	62 (22.1)	194 (69.0)		11 (5.1)	37 (17.3)	166 (77.6)	

†Fisher's exact test. SD, standard deviation.

Table 3. Factors that influence poor adherence to oral and topical medication

Oral medication	Atopic dermatitis, n = 177 (61.9%)	Urticaria, n = 75 (26.2%)	Psoriasis, n = 13 (4.5%)	Tinea, n = 21 (7.3%)	P
It felt like the symptoms had improved					
Yes	69 (39.0)	36 (48.0)	4 (30.8)	2 (9.5)	0.009
No	108 (61.0)	39 (52.0)	9 (69.2)	19 (90.5)	
Topical medication	**Atopic dermatitis, n = 349 (50.7%)**	**Urticaria, n = 124 (18.0%)**	**Psoriasis, n = 73 (10.6%)**	**Tinea, n = 143 (20.8%)**	**P**
It felt like the symptoms had improved					
Yes	122 (35.0)	36 (29.0)	24 (32.9)	45 (31.5)	0.650
No	227 (65.0)	88 (71.0)	49 (67.1)	98 (68.5)	

doctors' instructions were explored. As shown in Table 3, the rate of responses that "It felt like the symptoms had improved" varied significantly among the four skin diseases treated with oral medications. There was no significant difference in the rates of patient adherence to topical treatment plans among the four diseases.

DISCUSSION

Demographic data showed that at least 76.2% of patients suffered from chronic urticaria (for half a year or longer, Table 1), although the subtypes of urticaria (e.g. spontaneous or inducible) were unknown. Previous reports showed that approximately 70% of patients with urticaria suffered from the spontaneous type.[7,8] Therefore, at least half of the patients with urticaria in this survey could be classified as having chronic spontaneous urticaria. The proportion of female patients (66.4%) was approximately double that of the male ones (33.6%). In addition, the percentage of patients aged in their 30s to 50s, in the prime of life, was 82.3%. These demographic data are compatible with previous investigations on chronic urticaria.[9,10]

In our Web-based questionnaires, the patients were asked whether or not they had received medical treatment at a medical institution in the past year. The patients who answered that they had received medical treatment for atopic dermatitis, urticaria, psoriasis or tinea were asked the following additional question: "How much time has passed since you were diagnosed with that skin disease?". Thus, patients who answered this question might have included patients with acute urticaria. Because the symptom of acute urticaria resolves in a short time, these patients have fewer adherence-related problems, and may have better adherence to medication. Actually, in topical medication, patients with a disease duration of less than 6 months demonstrated significantly better adherence. However, in oral medication, no significant difference was observed in adherence between patients with different disease durations. This implies that patients with urticaria who require oral medication have poor adherence to medication irrespective of disease duration. In future study, we believe that we need to perform specific selection of patients with chronic spontaneous urticaria, in whom poor adherence is often observed (Table 2).

Adherence refers to patients actively participating in the therapeutic decision-making process and being treated accordingly.[11] Improving adherence via patient–doctor communication is essential for proper treatment. Common causes of poor adherence include a high frequency of medication administration, denial of the existence of an illness, a lack of understanding of the benefits of medication and cost.[12] In Europe, treatment in accordance with guidelines improved adherence, so the early application of guideline-based chronic urticaria management may be a cost-effective way to improve outcomes.[13]

For urticaria, the dose of oral medication (antihistamines) required for remission is dependent on the individual. Interminable treatment may lead to poor adherence. Among the four groups of dermatology patients (atopic dermatitis, urticaria, psoriasis and tinea), those with urticaria showed the poorest adherence, followed by those with atopic dermatitis.[4] Compared with patients with hypertension and diabetes, with whom comparative studies were conducted, patients with urticaria showed poorer adherence.[3,14] The reasons for such poor adherence are believed to be as follows: symptoms with fluctuating severity, the ease with which patients can stop treatment by themselves and low disease severity (not life-threatening). Although advances in Japanese health care have made treatment accessible at any time at low cost, atopic dermatitis and urticaria are diseases that significantly impair the quality of life of patients,[15] so poor adherence should not be ignored.

In conclusion, to improve adherence to urticaria treatment, patients should be aware of the importance of continuing oral medication for a certain period proactively, even if they do not have any symptoms. Concurrently, evidence is needed to show how long patients should continue oral medications depending on the severity and duration of urticaria. Furthermore, the evidence-based treatment guidelines for urticaria should be widely accepted by not only dermatologists, but also primary physicians.

ACKNOWLEDGMENTS: We asked MPR to run the administrative office for the present study, and would like to thank this

company for carrying out the questionnaire survey and collecting data. This study was financially supported by Mitsubishi Tanabe Pharma.

CONFLICT OF INTEREST: None declared.

REFERENCES

1 Hide M, Hiragun T. Japanese guidelines for diagnosis and treatment of urticaria in comparison with other countries. *Allergol Int* 2012; **61**: 517–527.
2 Zuberbier T, Asero R, Bindslev-Jensen C *et al.* EAACI/GA(2)LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria. *Allergy* 2009; **64**: 1417–1426.
3 Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. *J Clin Hypertens (Greenwich)* 2008; **10**: 348–354.
4 Furue M, Onozuka D, Takeuchi S *et al.* Poor adherence to oral and topical medication in 3096 dermatological patients as assessed by the Morisky Medication Adherence Scale-8. *Br J Dermatol* 2015; **172**: 272–275.
5 Saeki H, Imafuku S, Abe M *et al.* Poor adherence to medication as assessed by Morisky Medication Adherence Scale-8 and low satisfaction with treatment in 237 psoriasis patients. *J Dermatol* 2015; **42**: 367–72.
6 Cortina JM. What is coefficient alpha? An examination of theory and applications. *J Appl Psychol* 1993; **78**: 98–104.
7 Champion RH. Urticaria: then and now. *Br J Dermatol* 1988; **119**: 427–436.
8 Nettis E, Pannofino A, D'Aprile C, Ferrannini A, Tursi A. Clinical and aetiological aspects in urticaria and angio-oedema. *Br J Dermatol* 2003; **148**: 501–506.
9 Zuberbier T, Balke M, Worm M, Edenharter G, Maurer M. Epidemiology of urticaria: a representative cross-sectional population survey. *Clin Exp Dermatol* 2010; **35**: 869–873.
10 Gaig P, Olona M, Muñoz Lejarazu D *et al.* Epidemiology of urticaria in Spain. *J Investig Allergol Clin Immunol* 2004; **14**: 214–220.
11 World Health Organization. *Adherence to long-term therapies: Evidence for action*. World Health Organization, Geneva 2003; 107–114.
12 Richmond NA, Lamel SA, Braun LR *et al.* Primary nonadherence (failure to obtain prescribed medicines) among dermatology patients. *J Am Acad Dermatol* 2014; **70**: 201–203.
13 Conlon NP, Edgar JD. Adherence to best practice guidelines in chronic spontaneous urticaria (CSU) improves patient outcome. *Eur J Dermatol* 2014; **24**: 385–386.
14 Al-Qazaz HKh, Hassali MA, Shafie AA *et al.* The eight-item Morisky Medication Adherence Scale MMAS: translation and validation of the Malaysian version. *Diabetes Res Clin Pract* 2010; **90**: 216–221.
15 Staubach P, Eckhardt-Henn A, Dechene M *et al.* Quality of life in patients with chronic urticaria is differentially impaired and determined by psychiatric comorbidity. *Br J Dermatol* 2006; **154**: 294–298.